CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA

PROPICONAZOLE

Chemical Code # 2276, Tolerance # 434
SB 950 # Not Assigned

Original: 6/16/88 Revised: 10/23/89, 10/19/90, 1/22/03

I. DATA GAP STATUS

Combined (Chronic & Onco.), rat:	No data gap, no adverse effect
Chronic toxicity, rat:	No data gap (see combined)
Chronic toxicity, dog:	Data gap, inadequate study, no adverse effect indicated[1]
Oncogenicity, rat:	No data gap (see combined)
Oncogenicity, mouse:	No data gap, possible adverse effect
Reproduction, rat:	No data gap, no adverse effects
Teratology, rat:	No data gap, possible adverse effects
Teratology, rabbit:	No data gap, no adverse effects
Gene mutation:	No data gap, no adverse effects
Chromosome effects:	No data gap, no adverse effects
DNA damage:	No data gap, no adverse effects
Neurotoxicity:	Not required at this time

Toxicology one-liners are attached.
All record numbers through 157410 were examined.
** indicates an acceptable study.
Bold face indicates a possible adverse effect.

Updated by: J. S. Kishiyama and Gee, 1/22/03
Summary on Triazole Alanine, metabolite of Propiconazole, follows summary on Propiconazole.

[1] A replacement study is not being required because repeating the study at higher doses (>1000 ppm) would cause palatability problems before causing signs of toxicity (see SRSs of 1996). Gee, 1/22/03.

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

These pages contain summaries only. Individual worksheets may contain additional effects.

COMBINED, RAT

** 059 (4 parts) 62550 and 061 62552 "CGA 64,250: Potential Tumorigenic and Toxic Effects in Prolonged Dietary Administration to Rats." (Huntingdon Research Centre, England, HRC Report No. CBG 193/8284, 9/30/82.) CGA 64,250 (Propiconazole) technical (Batch No. P4-6, purity 87.2-91.9 %), administered at 0, 100, 500 or 2500 ppm in the diet to 80/sex/treatment level (50/sex/group for oncogenic assessments (no blood samples), ophthalmoscopy & hearing test; 10/sex/group for hematology; 10/sex/group for clinical chemistry and urinalyses; 10/sex/group for interim kill). Marginal liver changes in both sexes at high dose. **NO ADVERSE EFFECT.** Systemic NOEL = 100 ppm (decreased weight gain at 52 weeks). **ACCEPTABLE**. Margolis 4/5/88 and Gee, 4/19/88.

CHRONIC TOXICITY, RAT

See Combined, Rat

CHRONIC TOXICITY, DOG

067, 087, 092 62741, 74112, 74113, 87134 "One-Year Subchronic Oral Toxicity Study in Beagle Dogs with CGA64,250 Technical". (FDRL, Inc., Study No. 7737, 5/28/85.) CGA64,250 Technical (Propiconazole), 90.2% pure, was administered via feed at 0, 5, 50 or 250 ppm to groups of 7, 5, 5 or 7 beagles/sex, respectively. (Two dogs/sex from the control and high dose groups were retained for a 28 day recovery study). **NO ADVERSE EFFECT INDICATED.** NOEL $\geq$ 250 ppm. **UNACCEPTABLE**, No MTD was established and no adequate justification for dose level selection was given, submitted correspondence from EPA and the subchronic study (record 62341, doc. 434-017) do not adequately support dose selection. Possibly upgradable with an adequate justification for dose selection. Margolis, 3/24/88 and Gee, 4/20/88, revised 10/23/89 Morgan, updated 8/20/90, Morgan.

ONCOGENICITY, RAT

See Combined, Rat

ONCOGENICITY, MOUSE

**** 060 (3 parts), -062, -068 62551, 62754, 62755, 62742** "CGA64,250 Long-Term Feeding Study in Mice" (Final Report). (Huntingdon Research Centre, England, Rpt. No. CBG/196/81827, 10/26/82.) CGA64,250 (Propiconazole, 87-92% pure) was fed at 0, 100, 500 or 2500 ppm to 52 mice/sex/group for 104 weeks and to 12 mice/sex/group for 53 weeks (interim sacrifice). NOAEL = NOEL = 500 ppm. **POSSIBLE ADVERSE EFFECT** (significant incidence of neoplastic and non-neoplastic liver cell tumors in males at 2500 ppm). **ACCEPTABLE**. Margolis, 4/7/88 and Gee, 4/14/88, revised 10/17/89, Morgan, the original review indicated the NOAEL = 100 ppm, the data w analyzed using Fisher's Exact test and the NOAEL was found to be 500 ppm.

434 - 220 157410 Gerspach, R. "18-Month Oncogenicity Study in Mice." (Novartis Crop Protection, Inc. (formerly Ciba-Geigy Corp.), Stein, Switzerland, Laboratory Study Number 943126, 3/26/97). CGA 64250 Technical, purity 92.4%, was admixed with the feed at concentrations of 0, 100, 500, and 850 ppm (mg/kg food) and fed for 18 months to 50 male mice/group (with 30 additional mice/group for blood chemistry and interim sacrifices at 9 weeks and 12 months, 10/group). Doses were equivalent to 11.0, 59.0 and 107.6 mg/kg/day over the lifetime of the study. Overall NOEL = 100 ppm based on increased incidence of hepatocellular hypertrophy at 500 and 850 ppm; also, body weight gain retardation and liver weight increase were found. At the high dose, there was a statistically significant increase in adenomas (benign) but no increase in carcinomas. **(Possible adverse effect). SUPPLEMENTAL study.** The study was conducted to supplement the earlier study in which the 2500 ppm dose was too high. (Kishiyama and Gee, 1/22/03).

REPRODUCTION, RAT

** 066 (5 parts) 62757 "Two-generation Reproduction Study in Albino Rats with CGA 64,250 Technical." (American Biogenics Corporation (Previously--"Toxigenics, Inc."), Study No. 450-1202, 3/12/85.) CGA 64,250 (Propiconazole), (Lot # FL-830377, 89.7 % purity) was fed at 0, 100, 500 or 2500 ppm to 30 females and 15 males/generation (two parent generations with two litters each). Reproductive and parental NOEL = 500 ppm (body weights, pup survival). **NO ADVERSE REPRODUCTIVE EFFECTS**. **ACCEPTABLE**. Margolis, 4/26/88 and Gee, 4/28/88.

058 62607 "Report on CGA 64,250 Technical; 2-Generation Study" (Ciba Geigy Ltd., Basle, Switzerland, Test No. 79 0010, 6/29/81). CGA 64,250 (Technical Propiconazole), 91.9% pure, fed at 0, 400, 2000 or 5000 ppm via feed, to 10 F0 males and 20 F0 females/group, and 12 F1 males and 24 F1 females for each of the 0, 400 and 2000 ppm dose groups. 5000 ppm dose was discontinued due to 100 % perinatal mortality of the dams. **NO ADVERSE REPRODUCTIVE EFFECT INDICATED.** Provides data supplemental to # 62757. Nominal reproductive NOEL = 400 ppm; parental NOEL = 400 (body weight gain). **UNACCEPTABLE** (no diet analysis, no summary tables, no individual body weights, inadequate histopathology). Margolis, 4/25/88 and Gee, 4/29/88.

TERATOLOGY, RAT

** 017, 020, 087, 092 62338, 62356, 74116, 87133 "Teratology Study (Seg. II) in Rats." Ciba-Geigy, Basle, Switzerland, 9/10/79 (stability test reported 1/26/89); CGA 64 250 technical, 91.9%, given by oral gavage to 24 rats per group at 0 (2% carboxymethylcellulose), 30, 100 or 300 mg/kg/day, days 6 - 15 of gestation. Stability study indicated that dosage were stable for at least 4 hours; decreased weight gain approximately 6% and food consumption approximately 30% in the high dose group during dosing period with recovery; 3 "spontaneous" deaths at 300 mg/kg/day; increased incidence of absence of ossification in digit V of phalanges of the hindlimb and calcaneus in high dose fetuses; nominal maternal NOEL = 100 mg/kg/day, nominal developmental toxicity NOEL = 100 mg/kg/day. **NO ADVERSE EFFECTS INDICATED. ACCEPTABLE** (previously found unacceptable but possibly upgradable with submission of frequency of dose preparation to determine adequacy of the stability study. These data have been submitted and the dose solutions were found to be stable.) Gee, 4/18/88, updated Morgan, 10/23/89, revised 8/20/90, Morgan.

**** 093 87138** "Teratology (Segment II) Study Rats"; Crl:COBS CD (SD)BR Rat; Agricultural Division, Ciba-Geigy Corp., Summit, NJ.; 1/28/87; CGA 64250 Technical, Batch# FL 850083, stability and purity not stated; 0, 30, 90, 360/300 mg/kg/day oral gavage, dosed from gestational day 6-15 with 3.60% technical in 3% aqueous cornstarch with 0.5% Tween 80; 24 females/group (at 360/300 mg/kg/day 23 females were used); Number of fetuses: 270, 284, 302 and 285, respectively; 9311 historical control fetuses; 1 unscheduled death in the control group; Maternal toxicity included ataxia, lethargy and salivation; developmental toxicity included cleft palate, short or absent renal pappilla and dilated ureters; **Potential adverse effect: Cleft palate**; Maternal NOEL = 90 mg/kg/day, Developmental NOEL (cleft palate) = NOAEL(cleft palate) = 30 mg/kg/day; **Acceptable**. (Morgan and Chernoff, 8/27/90)

094 87139 "A Modified Teratology (Segment II) Study in Albino Rats with CGA-64250." Crl:COBS CD (SD)BR Rat; Pharmaceuticals Division, Ciba-Geigy Corp., Summit, NJ.; 2/6/87; CGA 64250 Technical, Batch# FL 850083, stability and purity not stated; 178 females in control group and 189 females in treated group, 300 mg/kg/day, oral gavage, dosed from gestational day 6-15 with 3.0% technical in 3% aqueous cornstarch with 0.5% Tween 80; 28 controls and 23 treated were not pregnant; 2122 control fetuses (155 litters), 2064 treated fetuses (158 litters), 9311 historical control fetuses; 3 unscheduled deaths in the treated group; Maternal toxicity included ataxia, lethargy, salivation and labored/audible respiration; developmental toxicity included decreased fetal weight and cleft palate; **Potential adverse effect indicated: Cleft palate**; Maternal NOEL < 300 mg/kg/day, Developmental NOEL (cleft palate and decreased fetal weight) = NOAEL(cleft palate) < 300 mg/kg/day; **Unacceptable and not upgradable**, only one dose level used, no fetal skeletal examination. (Morgan and Chernoff, 8/23/90)

TERATOLOGY, RABBIT

034 58461 "CGA 64,250 Technical: A Teratology Study in New Zealand White Rabbits." (Ciba-Geigy, NJ, 8/1/86, MIN 852172) Propiconazole technical, 92.1%, FL 850083; given by oral gavage to groups of 19 New Zealand White rabbits at 0 (3% cornstarch with 0.5% Tween 80), 100, 250 or 400 mg/kg/day, days 7 - 19 of gestation after artificial insemination; decreased food consumption and weight gain in the high dose with clinical observation especially in decreased stools, a smaller decrease in food consumption at 250 mg/kg; 5 abortions and 1 complete litter resorption at 400 mg/kg/day; NOEL = (maternal and developmental) = 250 mg/kg/day. **ACCEPTABLE. **No adverse developmental effect identified.** Gee, 4/15/88.

017, 020 62339, 62356 "Teratology Study (Seg. II) in Rabbits." (Ciba-Geigy, Basle, Switzerland, 9/10/79) CGA 64,250 technical, 91.9%; given by oral gavage to groups of 20 Chinchilla rabbits at doses of 0, 30, 90 or 180 mg/kg body weight per day, days 6 - 18 after mating; marginal effect of maternal body weight gain but significant reduction in food consumption during the dosing period; maternal NOEL = 90 mg/kg (food consumption); developmental toxicity NOEL = 90 mg/kg (skeletal variants in ossification). No malformations or other developmental toxicity noted. **NO ADVERSE EFFECTS INDICATED. UNACCEPTABLE AND NOT UPGRADABLE** (no analysis of dosing solution, no clinical observations in report, no evidence of an MTD) Gee, 4/15/88.

GENE MUTATION

017 087 062240 074114 "Salmonella/Mammalian-Microsome Mutagenicity Test - CGA 64250" (Ciba-Geigy Ltd., Basle, Switzerland, Test #782577, 1/4/79, revised 9/23/88) CGA 64250, 83.9% pure, Batch Jn 13/5 F 1+2; tested with Salmonella strains TA1535, TA1537, TA98 and TA100, with and without rat liver activation, triplicate plates, one trial, at 0, 25, 75, 225, 675 or 2025 mg/plate; **no adverse effects noted (no increase in reversion rate); originally reviewed and found unacceptable but upgradable with submission of individual plate counts, identification of test material by purity. (Gee 3/9/88) Reviewed again after submission of additional data (individual plate counts, purity of test material, Record #074114). **Status change** to **acceptable**. Klein and Gee 9/25/89

058, 063 62598, 62758 "L5178Y/TK$^{+/-}$ Mouse Lymphoma Mutagenicity Test." (Ciba-Geigy, 8/10/82) CGA 64,250 technical, propiconazole, batch op.103119 (90.7%); tested at 0 (DMSO), 7.81, 15.62, 31.25, 62.5 or 125 mg/ml, 4 hours incubation, with and without rat liver activation; 8 tubes each concentration for mutation frequency, 4 tubes for viability, single trial; individual tube counts in #62758; no increase in mutation frequency; **NO ADVERSE EFFECTS INDICATED. UNACCEPTABLE** (no confirming trial) - not upgradeable. Gee, 3/15/88.

058, 063 62600, 62760 "Point Mutation Assay with Mouse Lymphoma Cells - Host-Mediated Assay with CGA 64 250." (Ciba-Geigy, 8/10/82) Mouse lymphoma L5178Y cells injected intraperitoneally to 4 male mice/group at 106 cells/animal; three days after inoculation, animals were given 0 or 496 mg/kg orally; 3 days after administration, cells were harvested and tested for viability and mutation to resistance to cytosine arabinoside, methotrexate or thymidine; no effect on viability or mutation frequency was reported; NO **ADVERSE EFFECTS INDICATED. UNACCEPTABLE AND UPGRADABLE** with evidence that cells were exposed). Gee, 3/15/88.

CHROMOSOME EFFECTS

017 089 062336 074115 "Dominant Lethal Study, CGA 64250, Mouse (Test for cytotoxic or mutagenic effects on male germinal cells)" (Ciba-Geigy, Basle, Switzerland, Test # 790034, 10/31/79, revised 10/3/88) CGA 64250, Batch INA 35/1 (P 1), 90% pure, was given by oral gavage at 0, 165, or 495 mg/kg single dose to 20 NMRI-derived male mice; mated with 2 females each for 6 weekly periods; clinical signs in high dose males with recovery by day 2; **no adverse effects noted** (no evidence of a dominant lethal effect); originally reviewed as unacceptable (no description of test material, no concurrent or historical positive control data). (Gee 3/10/88) Reviewed again after submission of additional data (purity of test material, historical positive control data, Record # 074115). No status change, **unacceptable, possibly upgradable** (inadequate historical positive control data). Klein and Gee 9/25/89

017 62337 "Nucleus Anomaly Test in Somatic Interphase Nuclei - CGA 64 250 - Chinese Hamster (Test for Mutagenic Effects on Bone Marrow Cells)" (Ciba-Geigy, Basle, 9/17/79, No 79-0805) CGA 64 250, no purity stated, batch INA 35/1 (P 1), given by oral gavage at 0, 251, 502 or 1004 mg/kg, two daily doses to 6/sex/group, cyclophosphamide as positive control, sacrificed at 24 hours after second dosing; scored 3/sex/group for positive control and treated groups, 4 females and 2 males for vehicle control; one male died in high dose group but no cause of death given; **NO ADVERSE EFFECTS INDICATED. UNACCEPTABLE** and not upgradable (no purity stated, scored too few animals with no discussion, no clear evidence of adequacy of high dose, single sacrifice time.) No increase in micronuclei formation reported. Gee, 3/10/88

** 058, 063 62601, 62761 "Chromosome Studies in Male Germinal Epithelium - CGA 64,250 - Mouse (Test for Mutagenic Effects on Spermatogonia)." (Ciba-Geigy, 8/31/82) CGA 64 250 technical, propiconazole, batch op. 103119, 90.7%; given by oral gavage to male mice at 0, 166 or 498 mg/kg on five consecutive days (days 0, 1, 2, 3 and 4) with sacrifice on day five; 100 metaphases per animal were scored for chromosomal/chromatid aberrations, 8 animals in control and low dose group, 7 in high dose group (7 animals in high dose group died after first dosing); no increase in aberrations reported; NO **ADVERSE EFFECTS.** See also 62602, 62762. **ACCEPTABLE.** Gee, 3/16/88.

058, 063 62602, 62762 "Chromosome Studies in Male Germinal Epithelium - CGA 64 250 - Mouse (Test for Mutagenic Effects on Spermatocytes)" (Ciba-Geigy, 8/13/82) CGA 64 250 technical, propiconazole, batch op.103119. 90.7%; given by oral gavage to 15 male mice (NMRI-derived) per group at 0, 166 or 498 mg/kg, dosing on days 0, 2, 3, 5 and 9; animals sacrificed 3 days after last dosing; scored 100 spermatocytes I and II per animal, scoring metaphases from only 8 animals per group; no increase in aberrations in test animals reported; **NO ADVERSE EFFECTS INDICATED. UNACCEPTABLE AND NOT UPGRADABLE** (single sampling time, route of administration, inadequate description of procedure) Gee, 3/16/88.

DNA DAMAGE

058, 063 62599, 62759 "Saccharomyces cerevisiae D7/Mammalian-Microsome Mutagenicity Test in vitro with CGA 64 250." (Ciba-Geigy, 8/19/82) CGA 64 250, propiconazole, technical batch 103119, 90.7%; tested with Saccharomyces cerevisiae strain D7 (presumed diploid) with and without rat liver activation, 6 hours incubation at 0, 10, 30, 90 or 270 mg/ml; measured the following: Adenine requirement for mitotic crossing-over, tryptophan requirement for gene conversion and isoleucine requirement for back mutation; no evidence of an increase in any of the three parameters; concentration-dependent cytotoxicity; **NO ADVERSE EFFECTS. ACCEPTABLE. Gee, 3/15/88.

058, 063 62603, 62763 "Autoradiographic DNA Repair Test on Human Fibroblasts - CGA 64 250 (In vitro Test for DNA-Damaging Properties)." (Ciba-Geigy, 8/12/82) CGA 64 250 technical, propiconazole, batch op.103119, 90.7%; tested with human skin fibroblasts CRL 1121 without activation only; 0, 0.07, 0.37, 1.86 or 9.32 ug/ml, 5 hours in the presence of 3H-thymidine; 4 coverslips per concentration; scored 50 cells per coverslip for grain counts for a total of 200 cells; no evidence of unscheduled DNA synthesis; **NO ADVERSE EFFECTS**

INDICATED. UNACCEPTABLE AND NOT UPGRADABLE (no activation, normal DNA synthesis was not inhibited, concentrations not justified in the report with cytotoxicity data) Gee, 3/16/88.

058, 063 62604, 62764 "Autoradiographic DNA Repair Test on Rat Hepatocytes - CGA 64 250 (In vitro Test for DNA-Damaging Properties)" (Ciba-Geigy, 8/12/82) Propiconazole, CGA 64 250 technical, 90.7%, batch op. 103119; tested with primary rat hepatocytes for unscheduled DNA synthesis by autoradiography at 0, 0.67, 3.34, 16.69 or 83.47 mg/ml, 5 hours incubation in the presence of 3H-thymidine; no evidence for an increase in unscheduled DNA synthesis reported; **NO ADVERSE EFFECTS INDICATED. UNACCEPTABLE AND UPGRADABLE** with justification of the concentrations used and cytotoxicity data.) Gee, 3/16/88.

058, 063 62605, 62765 "Sister Chromatid Exchange Study - CGA 64 250 - Chinese Hamster (Test for Mutagenic Effects on Bone Marrow Cells)" (Ciba-Geigy, 10/18/1982) Propiconazole, CGA 64 250 technical, batch 103119, 90.7%; given by oral gavage to Chinese hamsters, 4/sex/group at 0, 255, 510 or 1050 (1/3 LD50), single dose; sacrificed at 24 hours; scored 25 metaphases of the second cycle per animal, scored only two animals per group; no increase in sister chromatid exchanges reported; dimethylbenzanthracene as positive control; **NO ADVERSE EFFECTS INDICATED. UNACCEPTABLE AND NOT UPGRADABLE** (inadequate number of animals scored, no MTD) Gee, 3/16/88.

058 62606 "Balb/3T3 Cell Transformation Assay - CGA 64 250 (In vitro Test for Transformation-inducing Properties in Mammalian Fibroblasts." (Ciba-Geigy, 8/10/82) Propiconazole, technical, 90.7%, batch op.103119, CGA 64 250; tested for ability to induce morphological transformation of mouse fibroblasts - Balb/3T3 cells; without activation only; 0 (vehicle and untreated), 1.16, 2.31, 4.63, 9.25 and 18.50 mg/ml, 72 hours incubation followed by 4 weeks of growth, 15 plates per concentration for transforming frequency and 3 plates at 200 cells each for viability after treatment; no evidence of increased transformation frequency resulting from treatment; **NO ADVERSE EFFECTS INDICATED. UNACCEPTABLE AND NOT UPGRADABLE** (no activation, no individual plate counts with no clear evidence of cytotoxicity to justify concentrations) - not upgradeable. Gee, 3/17/88.

NEUROTOXICITY

Not required at this time.

STUDIES ON TRIAZOLE ALANINE (METABOLITE OF PROPICONAZOLE)

Note: Triazole alanine is a metabolite (primarily occurring in plants) of a number of fungicides which contain the 1,2,4-triazole moiety, including Propiconazole. The CDFA Pest Management Library has assigned the metabolite a tolerance number of 50434. The most complete data package for this chemical has been submitted with Propiconazole, therefore, all relevant studies have been reviewed under Propiconazole's tolerance number -- 434.

A letter from Lois A. Rossi, Registration Division, U.S. EPA, dated March 30, 1988 [see folder], states that they have evaluated the toxicity data for triazole alanine and have determined that it "...exhibits a relatively low toxicity" and "...occur[s] naturally in plants at high levels relative to any contribution from the application of the subject pesticide." EPA is not requiring any additional studies on triazole alanine.

REPRODUCTION, RAT

073 062571 "Triazole Alanine: Two-Generation Reproduction Study in the Rat." (Imperial Chemical Industries PLC, 8/19/86.) Triazole alanine, 97.6%, from Bayer AG, Batch #TLB 1207/018-024, plant metabolite. 15 males and 30 females per group were fed 0, 500, 2000 or 10,000 ppm (1%) corrected for purity; analysis of diet indicated mean for 10,000 ppm to be 9586

ppm for the duration of the study with the range 8704 - 10520; two generations, two litters per generation; dose selection based on a preliminary study--high dose selected so nutrition would not be compromised; **NO ADVERSE EFFECTS INDICATED.** Reproduction and parental NOEL ≥ 10,000 ppm; Complete report but unacceptable to fill data gap for parent compound. Otherwise, follows guidelines. Supplemental data. NLH, 12/19/86 and Gee, 12/19/86 and 5/2/88.

070 62560, 62561 "Triazole Alanine: Rat multigeneration Study - Progress Report." (Imperial Chemicals Industries, UK, 9/83.) Triazole alanine (metabolite of Propiconazole), fed in the diet in the preliminary study at 0, 150, 625, 2500 or 10,000 ppm to 12 females and 6 males per group for 6 weeks then mated for one littering; parental animals and pups were sacrificed and necropsied; # 62560 is the preliminary study, #62561 is the 3-page progress report on first 3 weeks of full study at 0, 500, 2000 or 10,000 ppm with 15 males and 30 females per group; insufficient data to review for effects. **SUPPLEMENTAL DATA** on metabolite. Gee, 4/14/88.

TERATOLOGY, RAT

070 62559 "Triazole Alanine: Teratogenicity Study in the Rat." (Imperial Chemical Industries, UK, 10/13/83, report no CTL/P/875.) Triazole alanine (metabolite of Propiconazole), 94.8%; given by oral gavage to 24 female rats per group at 0 (water), 100, 300 or 1000 mg/kg body weight days 7 - 16 inclusive; no maternal effects at the high dose (limit test); no treatment related major defects; delayed ossification in several bones at 1000 mg/kg and to a lesser extent at 300 mg/kg/day; maternal NOEL ≥ 1000 mg/kg/day; developmental toxicity = 100 mg/kg/day (minor delays in ossification). **POSSIBLE ADVERSE EFFECT INDICATED** (delayed ossification). No individual data in report. Supplemental data on metabolite. Gee, 4/14/88.

GENE MUTATION

070 62553 "Salmonella/Microsome Test for Point Mutation Effect." (Bayer AG, 1/5/83, Report No. 11388) THS 2212, triazolylalanine (metabolite of Propiconazole), no purity stated; tested with Salmonella typhimurium strains TA1535, TA1537, TA1538, TA98 and TA100 with and without rat liver activation, 4 plates per concentration, two trials with each strain; 0, 20, 100, 500, 2500 or 12500 ug/plate; positive controls for activation were cyclophosphamide and 2-aminoanthracene, no positive control without activation; no increase in reversion rate; **SUPPLEMENTARY DATA** - test material a decomposition product/metabolite of parent compound. Gee, 3/10/88.

072 62567 "Point Mutation Test with Chinese Hamster Cells V79." (Ciba-Geigy, Basle, Switzerland, 7/11/86). Triazolylalanine (97.4%)- plant metabolite of Propiconazole; Tested ± S9 at 0 ,500, 1000, 2000, 4000, 6000, 8000 or 10,000 ug/ml, 21 hrs - S9 , 5 hrs + S9; No increase in mutation frequency; 18 plates per concentration, 2 trials. Complete. **SUPPLEMENTAL DATA** on metabolite. NLH, 12/9/88 and Gee, 12/18/86 and 4/29/88.

072 062570 "Salmonella/Mammalian-Microsome Mutagenicity Test, CGA 131,013 technical." (Ciba-Geigy, Basle, Switzerland, 7/11/86.) Triazole alanine (metabolite of Propiconazole), (CGA 131,013 technical, 97.4%, Batch TLB 1207 G. Lief) Strains TA1535, TA1537, TA98, TA100 and TA102 at 0, 20, 78, 313, 1250 and 5000 ug/0.1 ml with and without S9 (from Aroclor 1254

induced rats); No increase in reversion rate. Triplicate plates, two trials. **SUPPLEMENTAL DATA** on metabolite**.** NLH, 12/10/86 and Gee, 12/19/86 and 5/2/88.

CHROMOSOME EFFECTS

070 62554 "Micronucleus Test in CBC F1 Mice - TQM/4" (Imperial Chemical Industries, UK, 9/14/82) Triazole alanine (metabolite of Propiconazole), R152056, batch 02199/49, no purity stated, given by intraperitoneal injection at 0, 2500 or 5000 mg/kg to male CBC F1 mice (Balb/C females x CBA males), 15 per group with 5 from each sacrificed at 24, 48 and 72 hours; cyclophosphamide as positive control; scored 1000 polychromatic erythrocytes per animal and the number of normochromatic cells per 200 PCE's; no increase in micronuclei in animals treated with triazole alanine; **SUPPLEMENTAL DATA -** test material a decomposition product/metabolite of parent compound. Gee, 3/10/88.

070, 065 62555, 62767 "Micronucleus test for Mutagenic Effect on Mice." (Bayer AG, 8/9/82, Report 11054; 11054A, 7/8/83.) Triazole alanine (metabolite of Propiconazole), THS 2212, lot E238099, no purity stated; given by oral gavage to Bor:NMRI mice at 0 or 8000 mg/kg, single dose; 5/sex in vehicle control sacrificed at 24 hours, 15/sex in test group with 5/sex sacrificed at 24, 48 or 72 hours, cyclophosphamide as positive control with effect on micronuclei formation in the experimental groups; # 62767 contains the data comparing the scoring of micronuclei in the first and second 1000 polychromatic erythrocytes per animal at 24 hours and discussing the disparity in these counts for 1 male and 1 female, concluding the results are negative overall; **SUPPLEMENTARY DATA** on decomposition product/metabolite. Gee, 3/11/88.

072 062569 "Micronucleus Test (Chinese Hamster) (CGA 131,013 technical)" (Ciba-Geigy, Basle, Switzerland, 7/11/86.) CGA 131,013 technical (Triazole alanine, metabolite of Propiconazole), 97.4% at 5000 mg/kg by oral gavage to Chinese hamsters, 8/sex/group, sacrificed at 16, 24 & 48 hours post-treatment; no evidence for micronuclei formation. **SUPPLEMENTAL DATA** on metabolite. NHL, 12/9/86 and Gee, 12/18/86 and 5/2/88

DNA DAMAGE

070 62556 "Pol A_1^- Test on E. coli During Testing for Effects Harmful to DNA." (Bayer AG, 1/5/83, Report no. 11390.) Triazole alanine (metabolite of Propiconazole), THS 2212, no purity stated, tested with E. coli strains p3478 (pol A_1^-) and W3110 (pol A^+), with and without activation at 0, 62.5, 125, 250, 500 or 1000 ug/plate; the 1000 ug sample was a suspension; no difference in growth and no cytotoxicity was noted but table 1 of results is missing from the report; **SUPPLEMENTARY data** on decomposition product/metabolite of parent compound. Gee, 3/11/88.

070 62557, 62558 "Cell Transformation Test for Potential Carcinogenicity of R152056." (Huntingdon Research Centre, UK, 5/15/81.) Triazole alanine (metabolite of Propiconazole), no purity stated, was tested with BHK 21 C13 for ability to transform them to growth in soft agar; with activation, at 0, 1000, 2000, 4000, 8000 or 16000 mg/ml; without activation, at 0, 500, 1000, 2000, 4000 or 8000 mg/ml; length of exposure to the chemical unclear; duplicate plates for viability and for transformation frequency, single trial; authors of the report consider the results with activation as positive but BHK cells are sensitive to such growth conditions as density and when compared to control cells plated at lower densities to resemble actual survival after

treatment with the test material, the single value at the high concentration seems much less significant; **SUPPLEMENTARY DATA** on a decomposition product/metabolite of the parent compound. Gee, 3/11/88.

072 62568 "Autoradiographic DNA Repair Test on Rat Hepatocytes (CGA 131,013 Technical)"; (Ciba-Geigy, Basle, Switzerland, 7/11/86.) Triazole alanine (metabolite of Propiconazole), 97.4%, tested at 0, 0.08, 0.4, 2 or 10 mg/ml with rat hepatocytes, 5 hours; counted 150 cells per concentration, no evidence for unscheduled DNA synthesis; complete. **SUPPLEMENTAL DATA** on plant metabolite. NLH, 12/9/86 and Gee, 12/18/86 and 4/29/88.

065 62766 "Transformation/Liver-Microsome Test (In vitro Test for Transformation-inducing Properties in Mammalian Fibroblasts." (Ciba-Geigy, 9/12/84.) CGA 131 013, technical triazole alanine (metabolite of Propiconazole), no purity stated; tested with Balb/3T3 fibroblasts for transformation to morphological change; tested at 0 (solvent control and untreated control), 62.5, 125, 250, 500 or 1000 ug/ml with activation (24 hour incubation) and without activation (72 hour incubation); no evidence of increase in transformed foci; **SUPPLEMENTAL DATA** on decomposition product/metabolite. Gee, 3/11/88.